

Coronary Heart Disease and Diabetes Mellitus: Issues of Diagnosis, Drug and Surgical Treatment, Prognosis

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Abstract: Today, 2.1% of the world's population suffers from diabetes mellitus, and in 97% of cases it is type 2 diabetes mellitus (T2DM). Type 2 diabetes develops as a result of decreased insulin secretion β -pancreatic cells and decreased sensitivity of peripheral tissues to the hormone (insulin resistance). Analysis of incidence indicates that in the next decade the contribution of type 2 diabetes to overall mortality will increase and by 2030 will be 3.3% [1, 18]. Types 1 and 2 diabetes are associated with an increased risk of developing cardiovascular disease (CVD). Mortality from coronary heart disease (CHD) in men and women with diabetes is 2–3 and 3–5 times higher, respectively, than in patients of comparable age and gender without diabetes [2]. The share of CVD in the mortality structure of patients with diabetes is 80%, so the importance of their early diagnosis and aggressive treatment should be emphasized. A number of epidemiological studies have shown that in patients with diabetes, the incidence of CVD increases as glycemia increases [3, 4].

Pathogenesis of cardiovascular disorders in patients with diabetes

Currently, “non-traditional” risk factors for coronary artery disease in patients with type 2 diabetes include the level of insulinemia, the small size of LDL particles and the amount of apolipoprotein B found in all fractions of lipoproteins enriched with triglycerides. The effect of hyperglycemia on atherogenesis in the vascular wall is realized through the development of generalized dysfunction of the vascular endothelium, increased oxidative stress and increased concentrations of final glycosylated metabolic products. It is these processes in type 2 diabetes that sharply increase the adhesion of blood monocytes to the vascular endothelium with their subsequent penetration into the vascular wall. The process of monocyte-endothelial interaction is one of the main triggers for the formation of atherosclerotic plaque and the development of atherosclerotic lesions of the vascular wall.

The initial stage of the process is associated with the effect of oxidative stress on lipids circulating in the blood. Oxidized LPN, under the influence of chemotaxis, contacts monocytes, inducing an increase in the number of monocytes, their adhesion to the endothelium, and the penetration of monocytes into the vascular intima. Inside the vascular wall, monocytes, accumulating lipids, turn into foam cells, which, releasing active biological substances, play a central role in the formation of atheroma. The role of these cells is especially important in the secretion of proinflammatory mediators, under the influence of which endothelial cells increase the production of adhesion molecules, such as E-selectin, intercellular adhesion molecule I and vascular endothelial adhesion molecule I. These molecules further enhance the adhesion of circulating monocytes to the endothelium and the penetration of monocytes into the vascular intima. An increased level of endothelial cell adhesion and increased adhesion of monocytes to

the endothelium are characteristic of patients with type 2 diabetes [1, 7]. Thus, hyperglycemia provokes the emergence of primary foci of atheromatous damage to the vascular wall and creates conditions for the specific cellular component of these atheromas.

Of particular importance in type 2 diabetes are lipid metabolism disorders, which persist in these patients even after correction of blood glucose levels. These disorders are called diabetic dyslipidemia. Its components are hypertriglyceridemia, a decrease in the concentration of HDL cholesterol, and an increase in the percentage of small dense LDL particles. The lipid triad is a specific variant of atherogenic dislipoproteinemia, which contributes to the development of atherosclerosis, regardless of the increase in the levels of total cholesterol and total LDL fraction.

Lipotoxicity and increased levels of free fatty acids (FFA) in combination with hyperglycemia and/or insulin resistance serve as risk factors (RFs) for heart damage, since FFAs and their oxidation products have a direct toxic effect on the myocardium, which can cause the development of diabetic cardiomyopathy. Oxidized LDL is toxic to endothelial cells because it interferes with vasodilation through inactivation of nitric oxide and causes endothelial destruction.

Diagnosis of ischemic heart disease against the background of diabetes is often difficult. Features of diagnosing and assessing the severity of IHD against the background of diabetes include the fact that IHD in diabetes in men and women occurs at a younger age than in the absence of diabetes. Clinical manifestations of coronary artery disease in patients with diabetes are similar to those without diabetes. These include angina, silent ischemia, myocardial infarction and heart failure. In diabetes, coronary artery disease is often painless, which makes timely diagnosis and initiation of treatment difficult. Therefore, in patients with diabetes, screening studies for coronary artery disease should be more actively used, visualizing stress tests (stress echocardiography and radionuclide methods), Holter 24-hour ECG monitoring, computed tomography, especially with concomitant risk factors - hyperlipidemia, arterial hypertension (AH), obesity. Coronary angiography occupies the main place in the examination of patients with coronary artery disease, since it provides reliable information about the presence or absence of stenosis of the lumen of the coronary arteries, determines treatment options (drug or myocardial revascularization surgery) and the prognosis of the disease.

The examination plan for patients with diabetes with obvious signs of myocardial ischemia is similar to that for patients without diabetes. Indications for exercise testing, myocardial scintigraphy and coronary angiography are comparable. There is a growing interest in the study of radionuclide perfusion of the myocardium during stress tests and other methods for diagnosing latent myocardial ischemia in patients with diabetes [5]. There is evidence that such patients develop subclinical ventricular dysfunction, which has a negative impact on exercise capacity [6].

Treatment

Modern approaches to the treatment of patients with diabetes involve physiological glycemetic control (reducing the level of glycosylated (glycated) hemoglobin to 6.5% or less) and combating other risk factors for coronary artery disease, such as dyslipidemia, hypertension, obesity, smoking and nephropathy [7]. It has now been convincingly proven that close to normal glycemetic levels reduce mortality and the risk of complications in patients with diabetes 1 and 2.

Self-monitoring of blood glucose levels is important in the treatment of diabetes. It has been established that less than 10% of the total number of patients measure blood sugar regularly and only about 20% with sufficient frequency. Glycemetic control targets should be maintained at HbA1c levels <6.5%, fasting blood glucose levels <5.5 mmol/L and postprandial blood glucose levels <8 mmol/L (Table 1).

The modern definition of self-monitoring includes regularly self-measuring your blood glucose levels between doctor visits using a glucometer and using the results to adjust your diet, lifestyle, and glucose-lowering therapy regimen.

Drug treatment

Indications for standard therapy of coronary artery disease using nitrates, β -adrenergic blockers (BAB), calcium antagonists, antiplatelet agents (acetylsalicylic acid) and myocardial revascularization are the same in patients with and without diabetes [8–10]. To improve the life prognosis of a patient with coronary artery disease, the following drugs are used: aspirin (in the absence of contraindications); statins (regardless of initial cholesterol levels); angiotensin-converting enzyme (ACE) inhibitors - in cases where the patient has hypertension, heart failure, previous myocardial infarction or signs of left ventricular dysfunction, as well as beta blockers in cases where the patient has suffered a myocardial infarction and has heart failure. The main reasons for limiting the use of beta blockers in diabetes were considered to be that they have a negative effect on the glycemic profile, increase the risk of hypoglycemia and mask its manifestations. These adverse events are mainly characteristic of non-selective beta blockers (propranolol, etc.), which increase insulin resistance due to a decrease in insulin secretion mediated through β_2 receptors and reduce peripheral insulin-dependent glucose uptake. Highly selective beta blockers (bisoprolol, etc.) are devoid of these side effects and do not have negative effects on either insulin sensitivity or glucose metabolism. In these cases, patients with diabetes do not experience hypoglycemia and do not require dose adjustment of oral hypoglycemic drugs.

Considering the risk of developing hypoglycemia, which is dangerous for the cardiovascular system, in diabetes (especially with concomitant insulin therapy and taking non-selective blockers), the use of blockers in diabetes has its own characteristics. Thus, the first choice drugs are selective blockers (bisoprolol, metoprolol, nebivolol, etc.), the effect of which on glycemia is much less pronounced than that of non-selective drugs.

In their work, Jonas M. et al. [11] studied the use of beta blockers (of which 61% were selective) in a subgroup of high-risk patients who had type 2 diabetes in combination with coronary artery disease ($n = 2,723$). We assessed 3-year mortality in patients who received ($n = 911$; 33%) and did not receive ($n = 1,812$; 67%) beta blockers. Overall mortality during 3-year follow-up was 7.8% in patients who received beta blockers, compared with 14% in those who did not receive them (44% reduction). The reduction in cardiac mortality was 42% between the two groups of patients (4.9 vs. 8.4%, $p < 0.005$). Three-year survival curves showed a significant difference in patient mortality in the two groups ($p = 0.0001$). The results of multivariate analysis confirmed that beta blocker use was an independent factor in improving survival (relative risk = 0.58; 90% confidence interval, 0.46 to 0.74). Among the population of patients with diabetes, the best effect of beta blocker treatment was observed in elderly patients (aged 65 years and older), those with a history of myocardial infarction, those with limited functional ability to perform exercise, and those at low risk. Thus, beta blocker therapy improves long-term survival in high-risk patients with diabetes and coronary artery disease.

In Chen J. et al. [12] in a large group of elderly patients ($n = 45,308$) aged 65 years and older who had suffered a myocardial infarction and had no contraindications to the use of beta blockers, the use of this group of drugs for the purpose of secondary prevention of myocardial infarction led to a decrease in one-year mortality in patients with diabetes (similar to non-diabetic patients) and was not associated with an increase in diabetic complications.

After acute myocardial infarction in patients with diabetes, a favorable course of the disease was also noted when taking beta blockers. In a multivariate analysis of one-year survival after acute myocardial infarction, beta blockers were an independent predictor of a favorable prognosis for patients [13].

When prescribing beta blockers to patients with diabetes, preference should be given to drugs with cardioselective action that can be prescribed once a day, such as bisoprolol fumarate

(Concor, Takeda), i.e. modern selective beta blockers, which are well tolerated, proven to be highly effective and have sufficient safety in patients IHD. Due to its high selectivity, bisoprolol is well tolerated even in patients with relative contraindications to its use and rarely causes side effects. Bisoprolol (Concor) has virtually no effect on the smooth muscles of the bronchi, peripheral arteries, carbohydrate and lipid metabolism. Bisoprolol is effective and safe for diabetes, it does not affect blood glucose levels in patients with diabetes, and no dose adjustment is required when taking oral antidiabetic drugs. Regular and long-term treatment of hypertension, angina pectoris and chronic heart failure (CHF) with bisoprolol can not only reduce blood pressure to target levels, reduce the frequency of attacks and severe complications, but also improve the prognosis of patients' lives and increase its duration.

In a study conducted at the Institute of Cardiology. A.L. Myasnikov RKNPK, 30 patients with stage I or II hypertension and metabolic syndrome were prescribed bisoprolol (Concor) at a dose of 5 mg/day. Monotherapy with bisoprolol for 3 months led to a significant decrease in minimum systolic and diastolic blood pressure at night and did not cause significant changes in fasting plasma glucose and its postprandial level [14]. The metabolically neutral effect of bisoprolol allows it to be recommended to patients with concomitant disorders of carbohydrate and lipid metabolism.

In another study [15], bisoprolol therapy in 49 patients for 12 months did not worsen the course of type 2 diabetes, did not lead to an increase in insulin resistance and did not require increased glucose-lowering therapy even in patients with clinically manifest CHF II–III functional classes according to NYHA.

Prescribing bisoprolol can significantly improve the prognosis of life of patients with coronary artery disease and diabetes who undergo certain operations on the heart and blood vessels. Thus, it was shown that the administration of bisoprolol during and after CABG surgery significantly reduced the likelihood of death from any cause and the likelihood of non-fatal myocardial infarction in those patients who had a high risk of cardiovascular complications. In addition, treatment with bisoprolol is accompanied by a decrease in morbidity, improvement in the general condition of patients, and a decrease in mortality.

Thus, when using bisoprolol (Concor), an improvement in the general condition of patients and high safety of treatment are typical for high-risk patients, which include patients with a combination of coronary artery disease and diabetes. The drug bisoprolol is included in the Federal program of preferential drug provision for patients in the Russian Federation.

In the treatment of patients with diabetes, especially with concomitant atherosclerotic lesions of the arteries of the lower extremities, the non-selective beta blocker with α -blocking activity carvedilol is also successfully used. Thanks to the blockade α -1 receptors, the drug, in addition to its vasodilating effect, increases tissue sensitivity to insulin. It should be noted that patients with coronary artery disease and diabetes are especially prone to developing circulatory failure. It has been shown that in this group of patients, the first-line drugs are bisoprolol, metoprolol and carvedilol. Calcium antagonists (verapamil, diltiazem, amlodipine) effectively reduce blood pressure levels and, at the same time, the risk of adverse cardiovascular events in patients with diabetes. These drugs do not negatively affect carbohydrate and lipid metabolism.

In patients with coronary artery disease in combination with diabetes, trimetazidine can be an effective and safe addition to any antianginal drug with hemodynamic action. The anti-ischemic effect of trimetazidine is based on its ability to increase the synthesis of adenosine triphosphoric acid in cardiomyocytes with insufficient oxygen supply due to the partial redistribution of myocardial metabolism from the oxidation of fatty acids to a less oxygen-consuming pathway - glucose oxidation [6].

In the open multicenter study TRIMPOL-1 (Trimetazidin in Poland), the effectiveness and tolerability of a combination of trimetazidine and antianginal drugs (long-acting nitrates, calcium antagonists) was assessed in 50 patients with stable angina and type 2 diabetes. When taking

trimetazidine (60 mg/day) for 4 weeks, clinical parameters significantly improved: the frequency of angina attacks, the need for nitroglycerin, and exercise tolerance according to a stress ECG test on a treadmill [7]. If it is necessary to intensify antianginal therapy in patients receiving beta blockers, it is advisable to add trimetazidine.

ACE inhibitors are indicated for patients with diabetes with a confirmed diagnosis of CVD [1, 3], also for patients with diabetes accompanied by proteinuria and chronic kidney disease, given their proven nephroprotective effect [13]. When treated with ACE inhibitors, there is an improvement in glucose metabolism due to the ability of the drugs to increase the sensitivity of peripheral tissues to insulin. ACE inhibitors are especially indicated for patients with diabetes and coronary artery disease with signs of decreased contractile function of the left ventricle of the heart, i.e. they reduce the risk of developing cardiovascular events. ACE inhibitors reduce left ventricular hypertrophy and myocardial fibrosis, prevent myocardial remodeling, improve endothelial function and reduce insulin resistance. During treatment with ACE inhibitors, it is necessary to take into account that their administration to patients with diabetes receiving glucose-lowering therapy may increase the risk of hypoglycemic conditions.

The combination of diabetes and untreated hypertension is the most unfavorable factor in the development of coronary artery disease, stroke, heart and kidney failure. The recommended blood pressure level in patients with diabetes is <130/80 mmHg. Art. Achieving the target level of blood pressure in diabetes usually requires the combined use of various groups of antihypertensive drugs, primarily drugs related to inhibitors of the renin-angiotensin system. Identification and treatment of microalbuminuria and adequate blood pressure control with the use of ACE inhibitors and angiotensin II receptor blockers reduce cardiovascular complications. When choosing an antihypertensive drug in patients with type 2 diabetes, one should take into account not only its effect on microalbuminuria, but primarily on the risk of death.

In people with diabetes, in addition to hyperglycemia, there are additional risk factors for the development of unfavorable outcomes of coronary artery disease. Type 2 diabetes is usually accompanied by severe lipid metabolism disorders. Diabetes is most characterized by hypertriglyceridemia, which is also combined with low levels of high-density lipoprotein cholesterol (HDL-C) and a predominance of small, dense, easily oxidized particles of low-density lipoprotein cholesterol (LDL-C). These changes contribute to the development of atherosclerosis. Moreover, in combination with other risk factors, such as insulin resistance, hyperglycemia, hypertension and abdominal obesity, they contribute to pathological changes in the microvasculature, causing complications typical of diabetes,—diabetic retinopathy, neuropathy, damage to the arteries of the lower extremities [11]. Treatment of dyslipidemia in patients with diabetes should be carried out in accordance with the same principles as in patients with coronary artery disease: the priority is to achieve the target level of LDL-C, and among the drugs that can be used to reduce it are HMG-CoA reductase inhibitors (statins) are the first choice drugs [12]. When choosing a specific statin, it is necessary to be guided primarily by evidence-based medicine and take into account the long-term safety of treatment. In this regard, the best performance was observed for atorvastatin and rosuvastatin. Atorvastatin has high hypocholesterolemic activity and significantly reduces triglyceride levels.

All patients with type 1 diabetes with microalbuminuria and chronic kidney disease are recommended to reduce LDL-C levels (by at least 30%) by prescribing statins as the drug of choice (in some cases, combination therapy is indicated), regardless of the initial LDL-C concentration. In patients with type 2 diabetes in combination with CVD or chronic kidney disease over the age of 40 years, the target LDL-C level should be <1.8 mmol/l, and if there are no signs of CVD, then the LDL-C level should be less than 2.5 mmol /l.

Currently available data convincingly demonstrate the effectiveness of statins in the secondary prevention of coronary artery disease in patients with concomitant diabetes. Moreover, the degree of reduction in LDL-C levels is proportional to the degree of improvement in cardiovascular prognosis. For patients with diabetes who suffer from coronary artery disease, the

target level is total cholesterol <4.5 mmol/l (174 mg/dl), and LDL cholesterol <1.8 mmol/l (70 mg/dl). Taking into account that a decrease in the concentration of glucose in the blood can only slightly reduce the concentration of LDL-C, in patients with decompensated type DM and high levels of LDL-C in the blood, it is necessary to immediately carry out both glucose-lowering therapy and treatment with statins [7]. Table 1 presents therapeutic targets in patients with diabetes.

Other effects of statins - anti-inflammatory, antiplatelet and antioxidant, which do not depend on their hypocholesterolemic effect - can also affect cardiovascular risk.

If we focus only on fasting glucose levels, then 1/3 of patients with diabetes may not be diagnosed. Therefore, the early stages of hyperglycemia and asymptomatic diabetes are best diagnosed using an oral glucose tolerance test (taking 75 g of glucose), which gives an idea of both fasting glucose levels and 2 hours after exercise.

Recently, information has been received that the risk of developing diabetes (increased blood sugar and glycosylated hemoglobin (HbA1c) increases during statin therapy (especially when prescribing large doses). On the one hand, a study by the CTT group (Cholesterol Treatment Trilists Collaboration) showed that Diabetes patients taking statins live longer, with an average 10% reduction in mortality.³ On the other hand, there is evidence that long-term statin treatment for 5 years results in an average 9% increase in mortality. risk of developing hyperglycemia. Although this risk is negligible and it is unclear whether fasting hyperglycemia actually develops with diabetes, nevertheless, a corresponding warning has been included in the instructions for medical use of rosuvastatin since 2011. All scientific publications emphasize that such an effect exists, but today this should not affect treatment tactics. Therefore, patients with diabetes and patients with metabolic syndrome should receive statins precisely because the reduction in mortality from CVD is many times greater than the possible risk associated with hyperglycemia. In these cases, the absolute reduction in the risk of developing cardiovascular pathology outweighs the slight increase in the incidence of diabetes [10].

In the absence of an adequate effect from prescribing statins in patients with coronary artery disease and diabetes, combination therapy may be prescribed with the addition of ezetimibe (a bile acid sequestrant), long-acting nicotinic acid or fibrates to statins. Fibrates can be used as adjunctive therapy in situations where triglyceride and HDL-C levels are not adequately controlled with statin monotherapy [24]. Reducing triglyceride levels in patients with type 2 diabetes should begin with glycemic control. It is important to lose weight, reduce alcohol consumption and prescribe fibrates. The main advantages of combination therapy are: the ability to influence several parts of lipid metabolism, avoid high doses of statins, and reduce the incidence of side effects encountered when prescribing high doses of drugs.

Myocardial revascularization

Among patients with coronary artery disease, the proportion of patients with diabetes is increasing, many of whom undergo myocardial revascularization. With concomitant diabetes, widespread damage to the coronary arteries is usually observed, so it is necessary to bypass several vessels. In patients with coronary artery disease and diabetes, the risk of adverse outcomes, including death, is higher than in patients without diabetes, regardless of treatment strategy [5]. In addition, they have additional problems, such as a higher risk of restenosis and occlusion after percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). The advantages of PCI and CABG in this group of patients have been compared in several large randomized trials [8, 6, 14].

The BARI 2D study specifically examined the effectiveness of myocardial revascularization in patients with diabetes, most of whom had stable coronary artery disease [6]. The authors analyzed the results of coronary angiography and chose the most adequate method of revascularization—PCI or CABG. Then the patients were randomized and one group received only optimal medical therapy (OMT), and the other also received myocardial revascularization

along with OMT. At the screening stage, 4,623 patients were examined, approximately 50% of them were included in the study. During 5 years of follow-up, the total incidence of death, MI and stroke in patients receiving conservative treatment (12.2%) or undergoing myocardial revascularization (11.7%) did not differ significantly. In the sample of patients who underwent PCI, outcomes between invasive and non-invasive treatment (NIT) did not differ. In the subgroup of patients who underwent CABG, survival without cardiovascular complications after surgical treatment was significantly higher (77.6%) than with drug therapy (69.5%, $p = 0.01$), but survival between groups was significantly higher. did not differ (86.4 and 83.6%, $p = 0.33$).

In all randomized clinical trials (RCTs) in patients with diabetes, the rate of repeat revascularization after PCI (regardless of the type of stent - drug-eluting or bare stent) was higher than after CABG [7]. The results of a meta-analysis of 10 RCTs that studied the effectiveness of elective myocardial revascularization [34] confirmed the advantages of CABG over PCI in patients with diabetes in terms of improved survival. Five-year mortality was 20% after PCI and 12.3% after CABG (relative risk 0.70; 95% confidence interval 0.56–0.87), while among patients without diabetes there was no difference in mortality between these procedures. Thus, the relationship between the presence of diabetes and the type of revascularization was statistically significant.

Unfortunately, due to the chronic course of metabolic disorders in patients with diabetes, there is a constant progression of atherosclerosis, which leads to widespread myocardial ischemia against the background of damage to several coronary arteries and determines a high frequency of restenosis.

In the Russian Federation, perioperative data of 225 patients who underwent CABG in the Department of Cardiovascular Surgery of the IKK named after A.L. Myasnikov from May 2004 to December 2006. Patients with type 2 diabetes ($n = 125$) received drug therapy (hypoglycemic drugs or insulin) before surgery. Patients without diabetes were selected into the control group ($n = 114$). Based on the results of the work, the following conclusions were made. Patients with diabetes referred for CABG have a greater risk of intervention and more often suffer from diffuse damage to the coronary arteries. More pronounced damage to the coronary bed in this category of patients requires expanding the scope of surgical intervention. Decompensation of diabetes, coronary endarterectomy, and distal coronary artery disease were associated with a high risk of mortality and perioperative MI [8]. In this study, when high-dose oral antiplatelet drugs were used, routine addition of glycoprotein IIb/IIIa receptor blockers in patients with diabetes did not produce additional benefit. Even after successful revascularization, adequate control of cardiovascular risk factors and strict glycemic control are necessary. In further studies, the same authors showed that the incidence and mortality from IHD among patients with a combination of IHD and diabetes were higher than in patients without diabetes. In the group of patients with coronary artery disease with diabetes, compared with patients with coronary artery disease without diabetes, more pronounced calcification of the coronary arteries was observed, diffuse and distal lesions were more common, as well as more severe atheromatosis of the aorta, phlebopathy, and infectious complications occurred more often [2].

Forecast

The course of the disease in patients with coronary artery disease in combination with diabetes has a number of features.

1. The risk of developing coronary heart disease in patients with diabetes is increased by 3–5 times; the course of coronary artery disease against the background of diabetes depends more on the duration than on the severity of diabetes.
2. Complications of coronary artery disease develop earlier against the background of diabetes than in its absence; By age 50, 40–50% of patients with diabetes will experience at least one cardiovascular complication.
3. IHD against the background of diabetes in many cases proceeds asymptotically as silent myocardial ischemia up to painless MI [12].
4. IHD against the background of diabetes is often complicated by

unstable angina, myocardial infarction, and life-threatening cardiac arrhythmias. 5. In case of coronary artery disease against the background of diabetes, congestive heart failure develops faster, including after myocardial infarction [10]. 6. In case of coronary artery disease, patients with diabetes are often diagnosed with diffuse damage to the coronary arteries, including the distal parts of the coronary bed, which complicates PCI and coronary bypass surgery [12]. 7. According to intravascular ultrasound, in patients with coronary artery disease and diabetes, more pronounced atherosclerotic lesions and inadequate compensatory remodeling are observed in the coronary vessels [25]. Accelerated plaque progression, despite drug therapy, dictates the need for an aggressive anti-atherosclerotic strategy using statins in patients with diabetes [18].

Most patients with diabetes die from cardiovascular complications, which occupy a leading place among the causes of death. The combination of diabetes and coronary artery disease is unfavorable from the point of view of prognosis, especially with uncontrolled hyperglycemia. Non-drug preventive measures are important for this combined pathology: combating obesity, a sedentary lifestyle, quitting smoking, following a diet (significant limitation of quickly digestible carbohydrates, as well as animal fats, cholesterol) and maintaining an adequate lifestyle.

Conclusion

Comorbidity of somatic diseases in cardiological practice is one of the important prognostic factors influencing the outcome of the underlying disease. Patients with diabetes represent a high-risk group for developing coronary artery disease and other cardiovascular complications (cerebral strokes, peripheral vascular diseases). Of main importance for improving the prognosis of such patients is a complex pharmacological effect aimed at correcting glycemic levels, blood lipid levels, normalizing blood pressure, reducing myocardial ischemia, thrombogenic potential of the blood and factors of chronic nonspecific inflammation.

A number of studies have shown that in patients with type 2 diabetes, control of hyperglycemia alone prevents the development of mainly microvascular complications and has little effect on the prevention of macrovascular complications (myocardial infarction, stroke, peripheral arterial disease). To prevent the development of complications, the doctor must provide adequate therapy for hyperglycemia, hyperlipidemia and hypertension. Most patients are indicated for statin therapy due to convincing evidence obtained on reducing the risk of cardiovascular events in primary and secondary prevention, including mortality from coronary artery disease in patients with diabetes (CARDS, 4S, Health Protection Study) [6].

Literature

1. Abnormal orbitofrontal development due to prematurity / Gimenez M. Junque C., Vendrell P., Narberhaus A., Bargallo N., Botet F., Mercader J. M. // *Neurology*. 2006. Vol. 67, № 10. P. 1818
2. Alyward G. P. Outcome studies of low birth weight infants published in the last decade: A metaanalysis / Alyward G. P., Pfeiffer S. I., Wright A., Verhulst S. J. // *Journal of Pediatrics*. 1989. Vol. 115. № 4. P. 515—520.
3. Andersen S. L. Trajectories of brain development: point of vulnerability or window of opportunity? // *Neuroscience & Biobehavioral Reviews*, 2003. Vol. 27, № 1. P. 3—18.
4. Children born prematurely have atypical Sensory Profiles / Wickremasinghe A. C., Rogers E. E., Johnson B. C., Shen A., Barkovich A. J., Marco E. J. // *Journal of Perinatology*, 2013. Vol. 33. № 8. P. 631—635.
5. Contribution of Brain Size to IQ and Educational Underperformance in Extremely Preterm Adolescents [Electronic resource] / Cheong J. L., Anderson P. J., Roberts G., Burnett A. C., Lee K. J., Thompson D. K., Doyle L. W. // *PloS one*. 2013. Vol. 8 № 10. URL

6. Худоерова Дилноза Ризоевна// САХАРНЫЙ ДИАБЕТ В УСЛОВИЯХ ВИРУСНОЙ ПАНДЕМИИ COVID-19.// Analytical Journal of Education and Development //Volume: 02 Issue: 10 | Oct-2022
7. Худойорова Дилноза Ризоевна ГИПОТИРЕОЗ И СЕРДЕЧНО-СОСУДИСТЫЕ ЗАБОЛЕВАНИЯ
8. СОВРЕМЕННЫЙ ВЗГЛЯД НА ПРОБЛЕМУ// Journal of Advanced Research and Stability Volume: 02 Issue: 11 | Oct - 2022 P 160-163
9. Ведение Лечение диффузного Токсического Зоба У Пациентов С Эндокринной Оптольмопатией / Д.Р .Худоерова-Central Asian Journal of Medical and Natural Science 3(6), 339-342, 2022
10. Metabolic Syndrome in the context of Evolutionary Development, Modern Methods. KD Rizoevna INTERNATIONAL JOURNAL OF HEALTH SYSTEMS AND MEDICAL SCIENCES 1(6), 233-236, 2022
11. Худоёрова Дилноза Ризоевна //ОЖИРЕНИЕ В КОНТЕКСТЕ ЭВОЛЮЦИОННОГО РАЗВИТИЯ СОВРЕМЕННЫЕ МЕТОДЫ ДИАГНОСТИКИ И ЛЕЧЕНИЯ.// Analytical Journal of Education and Development // Volume: 02 Issue: 10 | Oct-2022 PP 403-407 .sciencebox.uz
12. Яхъяева Х.Ш. Сахарный диабет 2-го типа у детей и подростков бухарской области. // Биология и интегративная медицина 1 (48) 2021.—Р. 13
13. Syndrome of Throtoxicosis, Approaches to Diagnosis and Treatment KD Rizevna American Journal of Pediatric Medicine and Health Sciences (2993-2149) 1 (6...,2023
14. Диагностика И Лечение Аутоиммунный Тиреоидит ДР Худоёрова Research Journal of Trauma Disability Studies 2 (4), 85-94,2023
15. Сахарный Диабет У Ребенка ДР Худоёрова Research Journal of Trauma and Disability Studies 2 (8), 1-7,2023
16. Zhurakulova Zebuniso Ahtamovna. Secondary infertility in women of reproductive age with hypothyroidism|| ACADEMICIA: An International Multidisciplinary Research Journal|| 2022, Volume : 12, Issue: 5; p: 649-653 ISSN : 2249-7137 DOI : 10.5958/2249-7137.2022.00424.4
17. Шодиева Н. У. ОСОБЕННОСТИ ТЕЧЕНИЯ ВРОЖДЁННОГО ГИПОТЕРИОЗА И ЭФФЕКТИВНЫЕ МЕТОДЫ ДИАГНОСТИКИ //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2023. – Т. 3. – №. 4. – С. 191-198.
18. K., B. B., & N., Y. M. (2022). Peculiarities of the Development of Hypothiriosis in Women of the Climacteric Period. Central Asian Journal of Medical and Natural Science, 3(2), 333-338
19. Jurakulova Zebuniso Akhtamovna. PRIMARY INFERTILITY IN WOMEN OF REPRODUCTIVE AGEWITH HYPOTHYROIDISM // EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE. Vol. 2 No. 5 (2022) EJMP ISSN: 2795-921X. P 165-168
20. Самандаровна, И. Ш. . (2023). Влияние Дефицита Витамина D На Метаболические Параметры У Женщин С Ожирением. Research Journal of Trauma and Disability Studies, 2(7), 51–60.
21. Ahtamovna, Z. Z. . (2022). Diffusetoxic Goiter, Diagnosis and Treatment. INTERNATIONAL JOURNAL OF HEALTH SYSTEMS AND MEDICAL SCIENCES, 1(6), 331–336.